REMARKS

The Applicants respectfully request reconsideration of the present application in view of the foregoing amendments and in view of the reasons that follow.

I. Status of the Claims

Claims 1-2 and 12-21 are requested to be canceled.

Claims 3 and 7 are currently being amended. Support for the amendments can be found at page 35, lines 12-13; Table 1 at page 50; Table 3 at page 52.

This amendment adds, changes and/or deletes claims in this application. A detailed listing of all claims that are, or were, in the application, irrespective of whether the claim(s) remain under examination in the application, is presented, with an appropriate defined status identifier.

Because the foregoing amendments do not introduce new matter, entry thereof by the Examiner is respectfully requested. After amending the claims as set forth above, claims 3-11 are now pending in this application.

II. Claim rejection - 35 U.S.C. § 101

Claims 3-11 are rejected under 35 U.S.C. § 101 for allegedly lacking utility. Specifically, the Office Action asserts that even though MACP-2 expression has been found to be ***different*** (either up-regulated or down-regulated) in ***numerous types of cancer cells*** as compared to their non-cancerous counterparts, such a finding is NOT sufficient to conclude that MACP-2 has utility as a ***cancer marker***. (*See* Office Action at 3, 4, 7). The Office Action asserts that to have *utility*, a specific type of tumor or tumors must be identified, that the level of MACP-2 expression must be characterized, and that MACP-2 must be "*demonstrated*" as a diagnostic marker, or that MACP-2 be found "*accepted* as available for use as a diagnostic marker" for proliferative diseases (*i.e.*, cancer) (Office Action at 3, 4). In addition, the Office Action asserts that because no confirmed *in vivo* function of MACP-2 has

been identified, that MACP-2 can not be found to have utility. (Office Action at 7-8). The Applicants respectfully traverse the rejection and contend that these Office Action demands are far beyond what is needed to meet the utility requirement under U.S. patent law.

As noted in the Applicants' previous reply, to meet the utility requirement of 35 U.S.C. § 101, the Applicants need only show that the claimed invention is "***practically useful***," *Anderson v. Natta*, 480 F.2d 1392, 1397, 178 USPQ 458 (CCPA 1973), and confers a "***specific benefit***" on the public. *Brenner v. Manson*, 383 U.S. 519, 534-35, 148 USPQ 689 (1966). As acknowledged by the Federal Circuit, the utility threshold is not high:

> An invention is "***useful***" under section 101 if it is ***capable of providing some identifiable benefit***. See *Brenner v. Manson*, 383 U.S. 519, 534 [148 USPQ 689] (1966); *Brooktree Corp. v. Advanced Micro Devices, Inc.*, 977 F.2d 1555, 1571 [24 USPQ2d 1401] (Fed. Cir. 1992) ("to violate Section 101 the ***claimed device must be totally incapable of achieving a useful result***"); *Fuller v. Berger*, 120 F. 274, 275 (7th Cir. 1903) (test for utility is whether invention "is ***incapable of serving any beneficial end***"). (Emphasis added).

Further, while an asserted utility must be described with specificity, the patent the Applicants ***need not demonstrate utility to a certainty***. In *Stiftung v. Renishaw PLC*, 945 F.2d 1173, 1180, 20 USPQ2d 1094 (Fed. Cir. 1991), the United States Court of Appeals for the Federal Circuit explained:

> An invention need not be the best or only way to accomplish a certain result, and it need only be useful to some extent and in certain applications: ***"[T]he fact that an invention has only limited utility and is only operable in certain applications is not grounds for finding lack of utility***." *Envirotech Corp. v. Al George, Inc.*, 730 F.2d 753, 762, 221 USPQ 473, 480 (Fed. Cir. 1984).

However, the Office Action raises the utility threshold well beyond that recognized by the statute and the federal judiciary, requiring identification of specific tumor type(s), characterization of MACP-2 expression levels, proof that MACP-2 is accepted as a diagnostic marker, and a demonstration of the *in vivo* function of MACP-2. None of these requirements are necessary to meet the utility standard.

The examination guidelines for the utility requirement state that Office personnel are to adhere to the following.

> (B) Review the claims ***and supporting written description*** to determine if the applicant ***has asserted for the claimed invention*** any specific and substantial ***utility*** that is credible.
>
> (1) If the applicant has asserted that the claimed invention is useful ***for any particular practical purpose*** (*i.e.*, that it has a "specific and substantial utility") and the assertion would be ***considered credible by a person of ordinary skill in the art***, do not impose a rejection based on lack of utility. (MPEP §2107. II).

Here, the claimed invention relates to polynucleotides encoding SEQ ID NO:2 (MACP-2) that are "***associated with a cell proliferation disease***" (*e.g.*, **cancer**). The supporting written description provides ***numerous assertions*** of utility for the claimed polynucleotides, one of which is that such polynucleotides have utility ***as diagnostic markers for proliferative disease, such as cancer.*** As described previously, support for such a utility can be found in the specification at, for example: (1) page 14, lines 14-16, in Table 3, demonstrating that MACP-2 is expressed in tumor cells, and (2) page 34, line 20 through page 38, line 11, describing methods to utilize the claimed polynucleotides in diagnostic methods, and (3) particularly at page 34, lines 23-25, reciting that "the polynucleotides may be used to detect and quantitate gene expression in biopsied tissue in which expression of MACP may be correlated with disease." Moreover, use of the claimed polynucleotides as a diagnostic marker for a disease such as cancer is both a **specific** and **substantial** utility.

Also as previously described, the **credibility** of such a utility has been substantiated by the post-filing art. As is well appreciated, it is acceptable for an applicant to rely on post-filing date publications from other research groups to relate experimental data in lieu of experiments performed by the Applicants to substantiate an assertion of utility. In fact, abundant post-filing evidence demonstrates that MACP-2, now known as WIF-1, is associated with proliferative disease, including cancer, and that detection of aberrant expression of WIF-1 is indicative of cancer. The aberrant expression levels of WIF-1 (*e.g.*, increased expression level as compared to homologous non-cancerous tissue or decreased expression level as compared to homologous non-cancerous tissue) differs, however, between different types of cancer and different stages of disease. The Applicants once again provide post-filing evidence of increased MACP-2/WIF-1 expression associated with proliferative disease, particularly cancer. All publications have been previously provided.

WIF-1 **was expressed** in tissues samples from 5/6 human ovarian endometriod adenocarcinomas, but was ***not*** **expressed** in normal ovarian tissue. Therefore, WIF-1 is associated with endometroid adenocarcinomas and is a diagnostic marker for ovarian cancer. Steg *et al.*, "Multiple gene expression analysis in paraffin embedded tissues by TaqMan low-density array," *J. Molecular Diagnostics*, 8: 76-83 (2006)). Similar work in mice had also demonstrated that WIF-1 was **over-expressed** in ovarian granulosa cell tumors and in solid pretumoral lesions in the ovaries of mice, compared with normal ovarian tissue. Boerboom *et al.*, "Dominant-stable β-catenin expression causes cell fate alterations and Wnt signaling antagonist expression in a murine granulosa cell tumor model," *Cancer Res.*, 66: 1964-1973 (2006), *see* abstract and pages 1964 and 1966.

WIF-1 **over expression** has also been observed in other cancer types. Cebrat *et al.*, "Wnt inhibitory factor-1: a candidate for a new player in tumorigenesis of intestinal epithelial cells," *Cancer Lett.*, 206: 107-113 (2004), demonstrated that WIF-1 was over expressed in intestinal adenoma's compared to normal epithelial cells in APC mice, and was also over expressed in cell lines derived from murine and human mammary gland adenocarcinoma and human colon adenocarcinoma. *Id.* at page 107, 111. Using *lux* reporter construct, Reguart *et al.*, "Cloning and characterization of the promoter of human Wnt inhibitory factor-1,"

Biochem Biophys Res Comm., 323:229-234 (2004), demonstrated increased transcription in human cell lines derived from colon and non-small-cell lung cancers, but not from mesothelioma. Such results, demonstrating the association between **aberrant** WIF-1 expression and **proliferative disease** in humans and mice, support the credibility of a utility asserted in the specification.

In response to this data and post-filing art, the Office Action asserts that because there is "***no common thread of what types of tumors*** MACP-2 is present or over-expressed in" and because ***expression levels vary*** in the different tumors, MACP-2 has no utility as a cancer marker. (Office Action at 6). This is an inappropriate requirement for a finding of utility; there need not be a "common thread" defining the types of cancers in which MACP-2 is aberrantly expressed, nor must there be a well-defined expression profiled for each tumor type evaluated. The Office demands far more than what is necessary for a finding of utility. The data are clear: detection of aberrant MACP-2/WIF-1 expression in a ***variety of types of tumor cells*** is indicative of ***cancer*** in those cells; therefore, MACP-2/WIF-1 has utility a cancer marker in these cells. Such a utility is specific, substantial and credible.

Moreover, the *in vivo* function of MACP-2 has no bearing on its utility as a diagnostic marker for cell proliferative disease, and an explanation of exactly how MACP-2 affects other biomolecules (*i.e.*, the mechanism of action) is not required to establish utility. As noted above, the data are clear: detection of aberrant MACP-2/WIF-1 expression in a variety of types of tumor cells is indicative of cancer; therefore, MACP-2/WIF-1 has utility as a cancer marker.

Accordingly, the claimed invention meets the utility requirement under 35 U.S.C. § 101. First, the specification provides numerous examples of **specific** and **substantial** utilities, one of which is the use of the claimed polynucleotides as a diagnostic marker for proliferative disease such as cancer. The specification shows that MACP-2 is associated with cell proliferative diseased tissue, such as cancerous prostate tissue, and is also expressed in numerous other libraries derived from proliferative disease tissue. The specification also states that the polynucleotides may be used for diagnosing proliferative disorders associated

with expression of MACP such as cancer. Accordingly, a ***specific and substantial utility is asserted in the specification***. Second, as described in the post-filing art, the asserted utility *has been tested* by those skilled in the art and found ***credible***. Simply, the post-filing art illustrates that aberrant expression of MACP-2 is indicative of cancer in the cell types evaluated.

While the combination of data may not detail a mechanism of action of MACP-2, specify all tumor types or define specific MACP-2 expression levels in each cancer, such a showing is **not necessary** to establish the utility of an invention. As stated above, 1) utility need not be demonstrated to a certainty; 2) limited utility or operability in only certain applications is NOT grounds for finding lack of utility; and 3) all that is required is that one skilled in the art consider the asserted, specific and substantial utility **credible**. This bar for utility has clearly been exceeded by the present specification and supporting art. Thus, for at least these reasons, reconsideration and withdrawal of the rejection under 35 U.S.C. § 101 is respectfully requested.

III. Claim rejection – 35 U.S.C. § 112, first paragraph, enablement

Claims 3-11 are rejected under 35 U.S.C. § 112, first paragraph, allegedly because the "claimed invention is not supported by either a specific, substantial, and credible asserted utility, or a well established utility ... one skilled in the art clearly would not know how to use the claimed invention." (Office Action at 8). The Applicants respectfully traverse this ground for rejection.

Based on the arguments in the preceding section, the application supports an asserted substantial and credible utility for the claimed polynucleotides and therefore, the rejection under 35 U.S.C. § 112, first paragraph, for alleged lack of enablement has been rendered moot. Accordingly, the Applicants respectfully request reconsideration and withdrawal of this ground for rejection.

IV. Claim rejection – 35 U.S.C. § 112, first paragraph, written description

Claims 3-11 are rejected under 35 U.S.C. § 112, first paragraph, as allegedly containing subject mater which was not described in the specification in such a way as to reasonably convey to one skilled in the art that the inventors had possession of the invention at the time of filing. (Office Action at 8). Specifically, the Office Action asserts that the Applicants are not entitled to polynucleotides which encode polypeptides " "***associated with a cell proliferation***," based on the above ***utility*** rejection. (Office Action at 8). The Applicants respectfully traverse this ground for rejection.

Based on the arguments in the preceding section, the application supports an asserted substantial and credible utility for the claimed polynucleotides and therefore, the rejection under 35 U.S.C. § 112, first paragraph, for alleged lack of written description based on the utility rejection has been rendered moot.

Moreover, an applicant shows possession of the claimed invention by ***describing the claimed invention with all of its limitations*** using such descriptive means as words, structures, figures, diagrams and formulas that fully set forth the claimed invention." (MPEP § 2163:I). Here, the claimed invention with all of its limitations (polypeptides "***associated with cell proliferation disease***") is clearly described in words and in the tables provided in the specification as filed. First, it is well known that cancer is a cell proliferation disease. Even so, cancer is described as a cell proliferation disease in the specification at, for example, page 35, lines 12-20, stating that ***"[p]olynucleotide sequences encoding MACP*** may be used for the diagnosis of a ***disorder*** associated with expression of MACP. Examples of such a disorder include but are not limited to ... in particular, ***cancer***." Second, Tables 3 and 4 show that SEQ ID NO:2 is associated with cell proliferative disease; SEQ ID NO: 2 is expressed in ***prostate cancer tumor tissue*** (***proliferative disease tissue***) as well as libraries from other ***proliferative diseased tissues***. (See Table 1, page 50; Table 3, page 52; page 41 line 26 through page 42, line 17). As such, the claimed invention is fully described in the specification and one skilled in the art would clearly understand that the inventors were in possession of the invention at the time of filing.

For at least these reasons, the written description requirement of 35 U.S.C. § 112, first paragraph, are met, and reconsideration and withdrawal of the rejection is respectfully requested.

V. Conclusion

The present application is now in condition for allowance. Favorable reconsideration of the application as amended is respectfully requested.

The Examiner is invited to contact the undersigned by telephone if it is felt that a telephone interview would advance the prosecution of the present application.

The Commissioner is hereby authorized to charge any additional fees which may be required regarding this application under 37 C.F.R. §§ 1.16-1.17, or credit any overpayment, to Deposit Account No. 19-0741. Should no proper payment be enclosed herewith, as by a check or credit card payment form being in the wrong amount, unsigned, post-dated, otherwise improper or informal or even entirely missing, the Commissioner is authorized to charge the unpaid amount to Deposit Account No. 19-0741. If any extensions of time are needed for timely acceptance of papers submitted herewith, the Applicants hereby petition for such extension under 37 C.F.R. § 1.136 and authorizes payment of any such extensions fees to Deposit Account No. 19-0741.

Respectfully submitted,

Date July 12, 2007

By Stephanie H. Vavra 45,178

FOLEY & LARDNER LLP
Customer Number: 22428
Telephone: (202) 672-5538
Facsimile: (202) 672-5399

for Michele M. Simkin
Attorney for the Applicants
Registration No. 34,717